Table 1

Cells

Cell	Receptor
5.25	CXCR4, CD4, CCR5 (not expressed well) BONZO
5.25.Luc4.M7	CD4, CCR5, BONZO
HOS.CD4.CCR5	CD4, CCR5
HOS.CD4.CXCR4	CD4, CXCR4
HOS.CD4	CD4, low level expression of CCR5 and CXCR4
HOS HT4 R5 GFP wt	CD4, CXCR4, CCR5
HOS.CD4.CCR5.GFP.M7#6*	CD4, CXCR4, CCR5
P4.CCR5	CD4, CXCR4, CCR5
U87.CD4	CD4
U87.CD4 R5	CD4, CCR5
U87.CD4 X4	CD4, CXCR4
MT2	CD4, CXCR4
MT4	CD4, CXCR4
PM1	CD4, CXCR4, CCR5
CEM NKr CCR5	CD4, CXCR4, CCR5

Table 2 Representative viruses and reagents

Viruses	Envelope[a]	Source
89.6, SF2	R5-X4/SI/B	ARRRP[B]
92BR014,92US076	R5-X4/SI/B	ARRRP
JR-CSF, 91US005	R5/NSI/B	ARRRP
91US054	SI/B	ARRRP
NL43, MN, ELI	X4/B	ARRRP
92HT599	X4	ARRRP
92UG031	R5/NSI/A	ARRRP(IN-HOUSE)
92TH014, 92TH026	R5/NSI/B	ARRRP(IN-HOUSE)
92BR025, 93MW959	R5/SI/C	ARRRP(IN-HOUSE)
92UG035	R5/NSI/D	ARRRP(IN-HOUSE)
92TH022, 92TH023	R5/NSI/E	ARRRP(IN-HOUSE)
93BR020	R5-X4/SI/F	ARRRP(IN-HOUSE)
Antibodies	**Epitope**	**SOURCE**
Mabs 2F5, 1577	gp41 TM	ARRRP
Mabs IG1b12, 2G12, 17b, 48D	gp120 SU	ARRRP
Neutralization sera #2, HIV-IG	Polyclonal	ARRRP
Entry inhibitors	**Target**	**Source**
CD4-IG	gp120 SU	Genentech
CD4-IGG2	gp120 SU	Adarc
SCD4	Sigma	Progenics
T20 (DP178)	gp41 TM	Trimeris
Rantes, MIP1a/b	CCR5	SIGMA/ARRRP
SDF1a/b	CXCR4	SIGMA/ARRRP
AMD 3100	CXCR4	AnorMed
Dextran sulfate, Heparin	Non-specific	Sigma

[a]R5 (CCR5 co-receptor), X4 (CXCR4 co-receptor)
SI (syncytium inducing), NSI (non-syncytium inducing), A,B,C,D,E,F (envelope clade designation)
[b]AIDS Research and Reference Reagent Program

Table 3

Primers Tested for the Amplification of HIV Envelope	
RT PRIMERS	
RT env_N3	5'-GGA GCA TTT ACA AGC AGC AAC ACA GC-3'
RT env 9720	5' -TTC CAG TCA VAC CTC AGG TAC-3'
RT env 9740	5'-AGA CCA ATG ACT TAY AAG G-3'
5' PCR PRIMERS	
5'env	5' -GGG CTC GAG ACC GGT CAG TGG CAA TCA GAG TGA AG- 3'
5'env_Xho/Pin	5'-GGG CTC GAG ACC GGT GAG CAG AAG ACA GTG GCA ATG A-3'
5'env_START	5'-GGG CTC GAG ACC GGT GAG CAG AAG ACA GTG GCA ATG -3'
3' PCR PRIMERS	
3' env	5' -GGG TCT AGA ACG CGT TGC CAC CCA TCT TAT AGC AA- 3'
3'env_Xba/Mlu	5'-GGG TCT AGA ACG CGT CCA CTT GCC ACC CAT BTT ATA GC-3'
3'env_STOP	5'-GGG TCT AGA ACG CGT CCA CTT GCC ACC CAT BTT A-3'
3' delta CT	5' -GAT GGT CTA AGA CGC TGT TCA ATA TCC CTG CCT AAC TC- 3'
All Experiments are located in Virologic Book number 0188	

Table 4 (Panel 1)

Anti-HIV Drugs

Drug/Compound	Generic Name	Trademark	Manufacturer
RT Inhibitors (NRTI, nucleotide analogs)			
AZT, ZDV	**Zidovudine**	**Retrovir**	**Glaxo/Wellcome**
3TC	**Lamivudine**	**Epivir**	**Glaxo/Wellcome**
AZT + 3TC		**Combivir**	**Glaxo/Wellcome**
d4T	**Stavudine**	**Zerit**	**Bristol-Myers/Squibb**
ddI	**Didanosine**	**Videx**	**Bristol-Myers/Squibb**
ddC	**Zalcitabine**	**Hivid**	**Hoffman La Roche**
1592U89	**Abacavir**	**Ziagen**	**Glaxo/Wellcome**
AZT + 3TC + 1592U89		**Trizivir**	**Glaxo/Wellcome**
(-)FTC (5-fluoro-3TC; Corviracil)	Emtricitabine		Triangle Pharmaceuticals
(-)FTC + (+)FTC (50:50)	Racimir		QuadPharma
DAPD (DXG active)	Amdoxovir		Triangle Pharmaceuticals
F-ddA (2-fluoro-ddA)	Lodenosine		MedImmune Oncology (US Bioscience)
BCH-10652, dOTC (2-deoxy-3-oxa-4-thiocytidine)			BioChem Pharma, Inc.
D-d4FC			Triangle Pharmaceuticals (Schinazi)
RT Inhibitors (NTRTI, nucleotide analogs)			
bis-POC PMPA (GS-4331)	Tenofovir		Gilead Sciences
bis-POM PMEA (GS-840)	Adefovir dipivoxil		Gilead Sciences
RT Inhibitors (NNRTI, non-nucleosides)			
BI-RG-587	**Nevirapine**	**Viramune**	**Boehringer/Ingleheim (Roxanne)**
BHAP PNU-90152T	**Delavirdine**	**Rescriptor**	**Pharmacia & Upjohn**
DMP 266 (L-743,726)	**Efavirenz**	**Sustiva**	**Dupont Pharmaceuticals (Avid)**
MKC442 (Coactinon)	Emivirine		Triangle/Mitsubishi Kasei
AG-1549 (S1153) (on hold)	Capravirine		Agouron Pharmaceuticals
PNU-142721			Pharmacia & Upjohn
DPC-961, -963, -083, -08?			DuPont Pharmaceuticals
SJ-3366	Also entry inhibitor?		Samjin Pharmaceuticals
BHAP PNU-87201	Atevirdine		Upjohn
GW420867X (quinoxaline)	(2nd gen. HBY 097)		Glaxo/Wellcome (Hoechst Bayer)
TMC 120 (R147681)			Tibotec
TMC 125 (R165335)			Tibotec
R86183	tivirapine		Janssen Pharmaceuticals
Calanolide A			Sarawak Medichem Pharmaceuticals
Protease Inhibitors (PRI)			
Ro 31-8959	**Saquinavir-(hgc) Saquinavir-(sgc)**	**Invirase Fortivase**	**Hoffman-La Roche**
MK-639 (L-735,524)	**Indinavir**	**Crixivan**	**Merck Research Laboratories**
ABT-538 (A-84538)	**Ritonavir**	**Norvir**	**Abbott Laboratories**
AG1343	**Nelfinavir**	**Viracept**	**Agouron Pharmaceuticals**
141W94 (VX-478)	**Amprenavir**	**Agenerase**	**Glaxo-Wellcome/Vertex**
ABT-378/r	**Lopinavir/ritonavir**	**Kaletra**	**Abbott Laboratories**
BMS 232,632 (aza-peptide)			Bristol-Myers-Squibb
PNU-140690	Tipranavir		Pharmacia & Upjohn
DMP 450 (cyclic urea)	Mozenavir		Triangle/Avid (ph I/II)
TMC 126 (Erickson's compound)			Tibotec
GW433908 (VX-175)	amprenavir pro-drug		Glaxo/Wellcome/Vertex
L756,423 (on hold)			Merck
PD-178390 (dihydropyrone)			Parke Davis (Boehringer-Ingleheim)
? new candidate			Roche
DPC 681 and 684			DuPont Pharmaceuticals
AG-1776 (JE-2147 = KNI-764)			Agouron Pharmaceuticals
Envelope/Receptor Inhibitors			
T-20 (gp41)	Pentafuside		Trimeris Pharmaceuticals
T-1249 (gp41)			Trimeris Pharmaceuticals
D-peptide inhibitor (gp41) small mol.	SCH-C		Schering-Plough
AMD-3100 (CXCR4)	(bicyclam)		AnorMED
AMD-8664 (CXCR4)	(macrocyclam)		AnorMED
ALX40-4C (CXCR4)			U. PA
FP21399			Fuji Pharmaceuticals
PRO 542 (gp120)	CD4IgG2		Progenics Pharmaceuticals
PRO-140 (CCR5)	MAb CCR5		Progenics Pharmaceuticals
T-22 (CXCR4)	(peptide, 18-mer)		
Met-SDF-1 (CXCR4)			
TAK 779 (CCR5 antagonist)			Takeda
AOP-Rantes (CCR5)			Gryphon Sciences

Table 4 (Panel 2)

Rantes 9-68 (CCR5)			
CCR5 antagonists	4-(piperidin-1-yl) butane class		Merck
α-Immunokine-NNS03 (CCR5, CXCR4)	α-cobratoxin		PhyloMed Corp.
Integrase Inhibitors			
AR-177	Zintevir		Aronex Pharmaceuticals
Diketo acids			Merck Research Laboratories
Nucleocapsid Inhibitors			
RB 2121	cyclic peptide p7 mimic		(see PNAS 96:4886-4891 (1999))
CI-1012			Achelion Pharmaceuticals
RNase H Inhibitor			
SP1093V (BBNH Fe+3 derivative)			(Parniak)

FDA approved drugs are shown in boldface,red = discontinued development,blue = not sure about development status

Table 4 (Panel 3)

Generic Name (abbreviation)	Brand Name	Firm	FDA Approval Date
zidovudine, AZT	Retrovir	Glaxo Wellcome	March 87
didanosine, ddI	Videx	Bristol Myers-Squibb	October 91
zalcitabine, ddC	Hivid	Hoffman-La Roche	June 92
stavudine, d4T	Zerit	Bristol Myers-Squibb	June 94
lamivudine, 3TC	Epivir	Glaxo Wellcome	November 95
saquinavir, SQV, hgc	Invirase	Hoffman-La Roche	December 95
saquinavir, SQV, sgc	Fortovase	Hoffman-La Roche	November 97
ritonavir, RTV	Norvir	Abbott Laboratories	March 96
indinavir, IDV	Crixivan	Merck & Co., Inc.	March 96
nevirapine, NVP	Viramune	Boehringer Ingelheim	June 96
nelfinavir, NFV	Viracept	Agouron Pharmaceuticals	March 97
delavirdine, DLV	Rescriptor	Pharmacia & Upjohn	April 97
ZDV+3TC	Combivir	Glaxo Wellcome	September 97
efavirenz, EFV	Sustiva	DuPont Pharmaceuticals	September 98
abacavir, ABC	Ziagen	Glaxo Wellcome	February 99
amprenavir	Agenerase	Glaxo Wellcome	April 99
lopinavir/ritonavir	Kaletra	Abbott	September 2000
ZDV+3TC+ABC	Trizivir	GlaxoSmithKline	November 2000

CORECEPTOR ASSAY SCREEN TEMPLATE

active RLU limit: 100 tropism ratio limit: 5 CXCR4 CCR5 DUAL [redacted]

drug 1: L83
drug 2: AMD

	1			2			3			4			5			6		
	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4
No Drug RLU	34	26,471	0 00	14,140	55	257 09	46	6,849	0 01	21,656	38,144	0 57	30	7,336	0 00	3,988	31	128 65
L83 RLU		19,258		54				4,696		27	25,542			5,468		34		
AMD RLU		32		12,186				40		7,226	32			39		3,664		
	13			14			15			16			17			18		
	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4
No Drug RLU	4,552	19,102	0 24	149	226	0 66	67,389	72	935 96	611	19,715	0 03	46	3,948	0 01	284	4,330	0 07
L83 RLU	28	9,956		40	153		99			30	14,985			2,953		38	2,918	
AMD RLU	838	34		41	24		42,295			76	1,022			152		25	48	
	25			26			27			28			29			30		
	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4
No Drug RLU	67,828	68	997.47	14,982	12,020	1 25	3,788	4,384	0 86	50	37	[redacted]	658	242	2 72	231	35	6 60
L83 RLU	129			111	10,839		59	3,397					32	221		47		
AMD RLU	51,146			8,580	3,384		2,049	538					493	38		219		
	37			38			39			40			41			42		
	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4
No Drug RLU	100	39	[redacted]	3,724	2,310	1 61	450	668	0 67	148	24	6.17	32	22	[redacted]	60	61	[redacted]
L83 RLU				38	2,656		37	463		33								
AMD RLU				1,984	272		206	72		139								
	49			50			51			52			53			54		
	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4
No Drug RLU	35	107	0 33	83	4,209	0.02	18,099	8,451	2 14	39,257	38	1033.08	5,413	40	135 33	97,733	29	3370 10
L83 RLU		68			3,502		13,896	6,220		85			35			30		
AMD RLU		34			88		16,980	8,711		27,832			5,043			48,452		
	61			62			63			64			65			66		
	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4
No Drug RLU	3,769	40	94 23	786	48	16 38	340	21	16 19	5,189	43	120 67	4,318	37	116 70	196	51	3 84
L83 RLU	29			39			31			34			28			23		
AMD RLU	2,773			797			282			5,356			3,461			184		
	73			74			75			76			77			78		
	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4
No Drug RLU	391	26	15 04	98	38	[redacted]	4,449	28	158.89	4,357	9,102	0 48	6,090	105	58 00	1,886	3,635	0 52
L83 RLU	50						43			34	7,932		73	77		38	2,092	
AMD RLU	340						3,752			906	36		4,473	51		279	27	
	85			86			87			88			89			90		
	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4
No Drug RLU	510	33	15 45	979	59	16 59	491	33	14 88	300	3,815	0 08	297	3,615	0 08	39	61,594	0.00
L83 RLU	42			55			49			29	3,661		32	2,946			56,739	
AMD RLU	564			813			376			268	36		256	30			40	

	7			8			9			10			11			12		
	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4
No Drug RLU	30	1,217	0.02	49	1,128	0.04	42,206	70	602 94	45	1,159	0 04	44,589	97	459 68	32	29,118	0.00
L83 RLU		814			934		90				761		60				22,279	
AMD RLU		42			37		33,192				33		30,510				31	
	19			20			21			22			23			24		
	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4
No Drug RLU	100	5,204	0 02	11,299	52	217.29	1,273	20	63 65	7,375	10,856	0 68	4,397	7,130	0 62	16,115	50	322.30
L83 RLU		3,058		22			26			40	6,455		42	3,874		68		
AMD RLU		34		8,232			1,129			3,961	2,283		1,656	1,285		11,980		
	31			32			33			34			35			36		
	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4
No Drug RLU	53	974	0.05	177	32	5.53	24,739	33	749.67	612	45	13 60	2,997	9,695	0 31	416	31	13.42
L83 RLU		828		32			31			48			22	7,261		28		
AMD RLU		95		361			21,767			479			925	35		597		
	43			44			45			46			47			48		
	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4
No Drug RLU	45	338	0.13	714	45	15 87	11,029	18	612 72	2,908	43	67 63	13,997	52	269.17	24,377	34	716.97
L83 RLU		207		31			18			31			73			59		
AMD RLU		29		366			8,390			2,306			12,139			16,045		
	55			56			57			58			59			60		
	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4
No Drug RLU	9,254	23,846	0 39	5,249	20,393	0 26	470	39	12 05	19,175	126	152 18	513	31	16.55	3,264	28	116 57
L83 RLU	43	9,150		38	8,290		37			96	183		35			30		
AMD RLU	2,219	40		784	38		310			19,638	35		500			3,038		
	67			68			69			70			71			72		
	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4
No Drug RLU	3,853	77	50 04	411	34	12 09	7,857	41	191 63	25,437	38	669.39	17,443	45	387 62	16,707	38	439 66
L83 RLU	39			22			42			35			40			104		
AMD RLU	2,108			253			4,595			14,749			13,708			12,486		
	79			80			81			82			83			84		
	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4
No Drug RLU	263	38	6 92	3,890	9,577	0 41	2,089	1,698	1 23	475	43	11.05	8,475	38	223 03	4,107	33	124.45
L83 RLU	33			44	6,140		33	1,224		30			30			28		
AMD RLU	143			986	45		1,105	160		159			6,862			2,571		
	91			92			93			94			95			96		
	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4	R5	X4	R5:X4
No Drug RLU	443	13,452	0 03	34	128,238	0.00	22	62	[redacted]	45	33	[redacted]	43	42	[redacted]	46	35	[redacted]
L83 RLU	33	12,051			85,018													
AMD RLU	451	51			45													

Table 4B

	3		
	R5 cells	X4 cells	R5:X4
no drug			
R5 inhibitor			
X4 inhibitor			
%inhib by R5 inhibitor			
%inhib by X4 inhibitor			

	21		
	R5	X4	R5:X4
no drug			
R5 inhibitor			
X4 inhibitor			
%inhib by R5 inhibitor			
%inhib by X4 inhibitor			

DUAL or MIXED

DEAD

	76		
	R5	X4	R5:X4
no drug	14,982	12,020	1
R5 inhibitor	111	10,839	
X4 inhibitor	8,580	3,384	
%inhib by R5 inhibitor	99	10	
%inhib by X4 inhibitor	43	72	

	95		
	R5	X4	R5:X4
no drug	43	42	
R5 inhibitor			
X4 inhibitor			
%inhib by R5 inhibitor			
%inhib by X4 inhibitor			

Table 4C

Plate	Repeat	End time	Start temp.	End temp.	BarCode
1	1	6:39:36 PM	21.6	21.7	N/A

0.5 CPS (CPS)
18

26648	54	6970	37406	7158	38	1386	930	100	1184	112	30488
19248	262	72	18972	3478	3946	5010	46	14	11004	7474	60
106	9038	4002	32	238	26	976	34	38	48	9736	32
38	2000	528	16	16	36	298	52	14	54	52	38
122	2984	7264	40	38	20	23344	15340	44	156	40	32
36	52	28	40	28	40	62	32	38	22	44	28
22	32	28	9858	68	3802	46	11470	1958	42	42	24
30	64	36	3846	3390	57858	12620	126186	68	34	38	36

Plate	Repeat	End time	Start temp	End temp.	BarCode
2	1	6:41:51 PM	21.5	21.6	N/A

0.5 CPS (CPS)
34

26294	56	6728	38882	7514	24	1048	1326	40	1134	82	27748
18956	190	72	20458	4418	4714	5398	58	26	10708	6786	40
30	15002	4766	42	246	44	972	30	28	42	9654	30
40	2620	808	32	28	86	378	38	22	32	52	30
92	5434	9638	36	42	38	24348	25446	34	96	22	24
44	44	14	46	46	62	92	36	44	54	46	48
30	44	28	8346	142	3468	30	7684	1438	44	34	42
36	54	30	3784	3840	65330	14284	130290	56	32	46	34

Plate	Repeat	End time	Start temp	End temp	BarCode
3	1	6:44:06 PM	21.6	21.6	N/A

0.5 CPS (CPS)
16

18590	18	4306	23902	5386	30	924	894	32	660	48	23382
8698	148	34	14088	2880	3142	3160	40	46	7616	2842	32
30	10252	3542	38	172	34	842	30	32	44	7616	34
28	2396	370	28	26	66	172	32	22	28	36	26
64	3784	4822	32	28	24	6188	5702	34	120	34	24
16	28	62	26	28	30	38	38	38	44	62	34
38	52	40	7020	68	1798	62	7324	1076	50	42	32
32	50	70	3824	3138	53670	13088	104608	32	38	50	32

Plate	Repeat	End time	Start temp	End temp.	BarCode
4	1	6:46:20 PM	21.7	21.8	N/A

0.5 CPS (CPS)
24

19926	46	5086	27182	5550	26	704	974	32	862	44	21176
11214	158	42	15882	3026	2694	2956	26	20	5294	4906	44
56	11426	3252	82	270	52	814	36	40	64	6906	32
32	2916	556	42	30	64	242	38	24	36	42	40
72	3220	7618	36	38	44	12112	10878	32	246	32	42
32	48	22	30	28	24	136	30	56	34	24	24
32	38	40	8844	86	2386	54	4956	1372	50	46	28
22	34	40	3498	2754	59808	11014	65428	34	40	24	18

Plate	Repeat	End time	Start temp.	End temp.	BarCode
5	1	6:48:35 PM	21.9	21.9	N/A

0.5 CPS (CPS)
38

38	28	40	30	38	234	46	30	46	30	34	22
26	20	32	976	190	58	46	24	28	2298	1290	26
42	3260	420	50	36	34	102	26	34	24	40	24
28	378	88	32	34	32	40	42	54	26	30	48
36	62	11690	38	44	32	42	42	26	36	46	42
46	22	44	38	58	32	38	30	32	36	38	12
22	38	52	40	42	26	34	50	200	36	34	36
36	80	52	40	36	40	52	54	22	40	42	36

Plate	Repeat	End time	Start temp	End temp.	BarCode
6	1	6:50:50 PM	21.8	21.9	N/A

0.5 CPS (CPS)
30

26	28	40	34	40	50	38	44	34	36	40	40
42	28	32	1068	114	38	22	46	30	2268	1280	40
36	3508	656	48	40	34	88	30	34	56	30	36
28	166	56	28	18	40	18	38	32	34	26	32
32	114	5732	32	42	34	38	34	50	34	38	52
36	22	36	40	30	20	30	26	42	40	26	36
46	24	26	32	60	28	32	40	120	36	20	36
32	58	58	32	24	40	50	36	12	38	40	18

Plate	Repeat	End time	Start temp.	End temp.	BarCode
1	1	########	21.7	21.8	N/A

0.5 CPS (CPS)

32

24	14218	56	21586	28	4034	36	52	42088	40	43332	38
4780	174	71276	730	48	326	28	12022	1288	7198	4314	17856
69452	15306	4008	44	792	180	50	182	25292	718	3572	424
72	3922	546	128	44	66	30	900	11984	3194	16106	23794
30	88	18820	40438	4882	105946	8466	4934	470	20386	548	3376
3420	934	344	6268	5012	170	3546	504	8164	22214	15146	19592
344	82	5344	5330	6710	1880	338	4286	2112	466	7752	4078
580	1018	516	318	302	40	414	32	20	52	48	42

Plate	Repeat	End time	Start temp	End temp	BarCode
2	1	########	21.9	21.9	N/A

0.5 CPS (CPS)

22

44	14062	36	21726	32	3942	24	46	42324	50	45846	26
4324	124	63502	492	44	242	172	10576	1258	7552	4480	14374
66204	14658	3568	56	524	282	56	172	24186	506	2422	408
128	3526	354	168	20	54	60	528	10074	2622	11888	24960
40	78	17378	38076	5944	89520	10042	5564	470	17964	478	3152
4118	638	336	4110	3624	222	4160	318	7550	28660	19740	13822
438	114	3554	3384	5470	1892	188	3494	2066	484	9198	4136
440	940	466	282	292	38	472	36	24	38	38	50

Plate	Repeat	End time	Start temp.	End temp	BarCode
3	1	########	21.9	22	N/A

0.5 CPS (CPS)

36

36	38	28	28	38	28	36	42	114	40	60	46
32	34	80	26	16	36	30	18	26	30	48	80
126	106	34	42	30	46	22	26	32	58	8	28
26	46	42	38	34	20	18	34	24	36	100	60
28	146	15756	76	32	26	42	52	36	106	34	24
34	50	20	24	32	18	38	18	36	38	50	58
38	38	28	36	80	50	38	44	34	38	30	28
40	30	38	30	24	22	38	36	34	36	22	26

Plate	Repeat	End time	Start temp	End temp	BarCode
4	1	########	21.9	22	N/A

0.5 CPS (CPS)

16

24	70	30	26	26	40	18	32	66	30	60	34
24	46	118	34	26	40	34	26	26	50	36	56
132	116	84	34	34	48	34	38	30	38	36	28
32	30	32	28	26	40	46	28	12	26	46	58
34	84	12036	94	38	34	44	24	38	86	36	36
24	28	42	44	24	28	40	26	48	32	30	150
62	24	58	32	66	26	28	44	32	22	30	28
44	80	60	28	40	28	28	34	32	36	18	28

Plate	Repeat	End time	Start temp.	End temp	BarCode
5	1	########	22	22	N/A

0.5 CPS (CPS)

34

38	11132	26	6696	34	3960	44	40	29548	40	30628	34
762	48	39888	88	40	30	36	8416	1262	4096	1598	12372
52058	8050	2524	60	450	168	32	340	22410	534	1046	512
106	2080	172	170	38	38	30	444	7478	2458	10024	15470
30	46	16428	25792	4240	45094	2092	630	334	17130	388	2730
2498	732	358	5044	3236	202	2124	292	4806	13736	13012	12386
290	30	3986	886	4584	240	110	940	1286	162	6768	2204
456	816	438	294	260	44	524	40	34	22	38	20

Plate	Repeat	End time	Start temp	End temp	BarCode
6	1	########	22	22.1	N/A

0.5 CPS (CPS)

32

40	13240	38	7756	38	3368	24	40	36836	48	30392	36
914	34	44702	64	50	20	24	8048	996	3826	1714	11588
50234	9110	1574	46	536	270	20	382	21124	424	804	682
200	1888	240	108	28	46	30	288	9302	2154	14254	16620
46	28	17532	29872	5846	51810	2346	938	286	22146	612	3346
3048	862	206	5668	3686	166	2092	214	4384	15762	14404	12586
390	64	3518	926	4362	318	176	1032	924	156	6956	2938
672	810	314	242	252	26	378	30	20	34	50	38

Patient Sensitivity Table 4E

R5

No Drug

34	14,140	46	21,656	30	3,988	30	49	42,206	45	44,589	32
4,552	149	67,389	611	46	284	100	11,299	1,273	7,375	4,397	16,115
67,828	14,982	3,788	50	658	231	53	177	24,739	612	2,997	416
100	3,724	450	148	32	60	45	714	11,029	2,908	13,997	24,377
35	83	18,099	39,257	5,413	97,733	9,254	5,249	470	19,175	513	3,264
3,769	786	340	5,189	4,318	196	3,853	411	7,857	25,437	17,443	16,707
391	98	4,449	4,357	6,090	1,886	263	3,890	2,089	475	8,475	4,107
510	979	491	300	297	39	443	34	22	45	43	46

L83

30	54	29	27	32	34	27	37	90	35	60	40
28	40	99	30	21	38	32	22	26	40	42	68
129	111	59	38	32	47	28	32	31	48	22	28
29	38	37	33	30	30	32	31	18	31	73	59
31	115	13,896	85	35	30	43	38	37	96	35	30
29	39	31	34	28	23	39	22	42	35	40	104
50	31	43	34	73	38	33	44	33	30	30	28
42	55	49	29	32	25	33	35	33	36	20	27

AMD

39	12,186	32	7,226	36	3,664	34	40	33,192	44	30,510	35
838	41	42,295	76	45	25	30	8,232	1,129	3,961	1,656	11,980
51,146	8,580	2,049	53	493	219	26	361	21,767	479	925	597
153	1,984	206	139	33	42	30	366	8,390	2,306	12,139	16,045
38	37	16,980	27,832	5,043	48,452	2,219	784	310	19,638	500	3,038
2,773	797	282	5,356	3,461	184	2,108	253	4,595	14,749	13,708	12,486
340	47	3,752	906	4,473	279	143	986	1,105	159	6,862	2,571
564	813	376	268	256	35	451	35	27	28	44	29

X4

No Drug

26,471	55	6,849	38,144	7,336	31	1,217	1,128	70	1,159	97	29,118
19,102	226	72	19,715	3,948	4,330	5,204	52	20	10,856	7,130	50
68	12,020	4,384	37	242	35	974	32	33	45	9,695	31
39	2,310	668	24	22	61	338	45	18	43	52	34
107	4,209	8,451	38	40	29	23,846	20,393	39	126	31	28
40	48	21	43	37	51	77	34	41	38	45	38
26	38	28	9,102	105	3,635	38	9,577	1,698	43	38	33
33	59	33	3,815	3,615	61,594	13,452	128,238	62	33	42	35

L83

19,258	32	4,696	25,542	5,468	28	814	934	32	761	46	22,279
9,956	153	38	14,985	2,953	2,918	3,058	33	33	6,455	3,874	38
43	10,839	3,397	60	221	43	828	33	36	54	7,261	33
30	2,656	463	35	28	65	207	35	23	32	39	33
68	3,502	6,220	34	33	34	9,150	8,290	33	183	33	33
24	38	42	28	28	27	87	34	47	39	43	29
35	45	40	7,932	77	2,092	58	6,140	1,224	50	44	30
27	42	55	3,661	2,946	56,739	12,051	85,018	33	39	37	25

AMD

32	28	40	32	39	142	42	37	40	33	37	31
34	24	32	1,022	152	48	34	35	29	2,283	1,285	33
39	3,384	538	49	38	34	95	28	34	40	35	30
28	272	72	30	26	36	29	40	43	30	28	40
34	88	8,711	35	43	33	40	38	38	35	42	47
41	22	40	39	44	26	34	28	37	38	32	24
34	31	39	36	51	27	33	45	160	36	27	36
34	69	55	36	30	40	51	45	17	39	41	27

T20 Resistance Mutations

SDM Virus	T20 Sens.[a]	T20 FC[b]
HXB2 G I V		1.0
NL4-3 G I V	S	5.2
NL4-3 D I V	S	12.8
NL4-3 G I M	S	33.0
NL4-3 S I V	S	74.2
NL4-3 D I M	R	113.0
NL4-3 S I M	R	227.4
NL4-3 D T V	R	>281.8
JRCSF G I V		2.1
JRCSF D I V		104.0

[a] Rimsky et al., J. Virol. 72(2):986-993

[b] Fold change in IC50 (vs. HXB2) using PhenoSense HIV Entry Assay

T20 Resistance Mutations

SDM Virus	T20 Sens.[a]	T20 FC[b]
HXB2 G I V		1.0
NL4-3 G I V	S	5.2
NL4-3 D I V	S	12.8
NL4-3 G I M	S	33.0
NL4-3 S I V	S	74.2
NL4-3 D I M	R	113.0
NL4-3 S I M	R	227.4
NL4-3 D T V	R	>281.8
JRCSF G I V		2.1
JRCSF D I V		104.0

[a] Rimsky et al., J. Virol. 72(2):986-993
[b] Fold change in IC50 (vs. HXB2) using PhenoSense HIV Entry Assay

Table 6

Entry Inhibitor Susceptibility: T-20 Fusion Inhibitor

Drug resistance mutations were introduced into well-characterized X4 tropic (NL4-3) and R5 tropic (JRCSF) viruses. T20 susceptibility was measured using the virus entry assay. The fold change (FC) in T-20 susceptibility for each virus was determined by dividing the IC50 of the test virus by the IC50 of the HXB2 strain of HIV-1. T-20 sensitivity of similar mutant viruses has been reported in the scientific literature (Rimsky et al.,).

Table 7

Identifying Entry Inhibitor Resistance Mutations

Virus	AA Sequence[a]											
HXB2	Q	L	L	S	G	I	V	Q	Q	Q		
1	Q	L	L	S	G	I	V	Q	Q	Q		
2	Q	L	L	S		I		Q	Q	Q		
3	Q	L	L	S	X	I	X	Q	Q	Q	X=G/S	X=V/M
4	Q	L	L	S	G	I	V	Q	Q	Q		
5	Q	L	L	S	G	I	V	Q	Q	Q		
6	Q	L	L	S	X	I	X	Q	Q	Q	X=G/S	X=V/M
7	Q	L	L	S	G	I	V	Q	Q	Q		
8	Q	L	L	S	G	I	V	Q	Q	Q		
9	Q	L	L	S	G	I	V	Q	Q	Q		
10	Q	L	L	S		I	V	Q	Q	Q		
12	Q	L	L	S	X	I	V	Q	Q	Q	X=G/D	
13	Q	L	L	S	G	I	V	Q	Q	Q		

[a] gp41 amino acid sequence positions 32 to 41

Identifying Entry Inhibitor Resistance Mutations

Virus	AA Sequence[a]											
HXB2	Q	L	L	S	G	I	V	Q	Q	Q		
1	Q	L	L	S	G	I	V	Q	Q	Q		
2	Q	L	L	S	S	I	M	Q	Q	Q		
3	Q	L	L	S	X	I	X	Q	Q	Q	X=G/S	X=V/M
4	Q	L	L	S	G	I	V	Q	Q	Q		
5	Q	L	L	S	G	I	V	Q	Q	Q		
6	Q	L	L	S	X	I	X	Q	Q	Q	X=G/S	X=V/M
7	Q	L	L	S	G	I	V	Q	Q	Q		
8	Q	L	L	S	G	I	V	Q	Q	Q		
9	Q	L	L	S	G	I	V	Q	Q	Q		
10	Q	L	L	S	D	I	V	Q	Q	Q		
12	Q	L	L	S	X	I	V	Q	Q	Q	X=G/D	
13	Q	L	L	S	G	I	V	Q	Q	Q		

[a] gp41 amino acid sequence positions 32 to 41

Table 7

Identifying Envelope Protein Mutations.

Viruses with reduced (or increased) susceptibility to an entry inhibitor are identified using the virus entry assay. Mutations that may confer reduced (or increased) susceptibility to the entry inhibitor are identified by sequencing the envelope genes of the sensitive and resistant viruses. The deduced amino acid sequences of the sensitive and resistant viruses are compared to identify candidate drug resistance mutations. The ability of a specific mutation to confer altered drug susceptibility is confirmed or disproved by introducing the mutation into a drug sensitive virus and measuring the susceptibility of the mutant virus in the virus entry assay. In the example represented here, a short stretch of amino acid sequences within the first heptad repeat (HR-1) of the HIV-1 gp41 transmembrane envelope protein is aligned for viruses exhibiting different T-20 susceptibilities. Highlighted amino acids represent mutations known to confer reduced susceptibility to T-20.

Similar analyses can be used to identify envelope amino acid sequences that (a) alter/influence susceptibility to CCR5 or CXCR4 inhibitors, (b) specify X4, R5 and dual tropism, and © elicit neutralizing antibodies.

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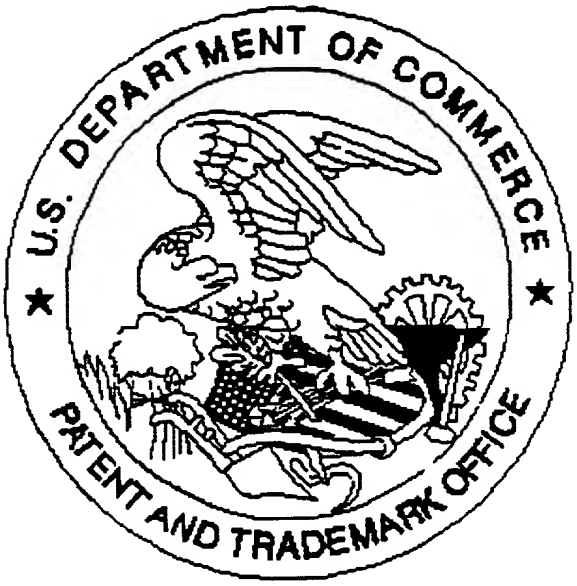

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